MAY 17 2004

K033745

4.0 510(K) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: **K033745**

1. Establishment

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Contact: William J. Radvak
President and CEO

Prepared: November 27, 2003

2. Regulatory Information

Trade Name:	**Response Biomedical Corp. RAMP® Troponin I Assay**
Common Name:	Troponin I immunological test system
Classification Name:	Troponin I immunological test system
Regulation Number:	**862.1215**
Product Code:	**MMI**
Panel:	**Clinical Chemistry**

3. Predicate Device

Immunoassay:	Triage Cardiac Panel®; Troponin I Assay (K973126) which is currently being marketed by Biosite Diagnostics, Inc.
Immunoassay:	Dimension® RxL Cardiac Troponin-I Flex®, (K973650) which is currently being marketed by Dade Behring Inc.

4. Description of the Device

The RAMP Troponin I Assay is a quantitative immunochromatographic test for the determination of TnI levels in EDTA whole blood. Diluted EDTA whole blood is added to the sample well of the Test Cartridge which houses the immunochromatographic test strip. The red blood cells are retained in the sample pad, and the separated plasma migrates along the strip. Fluorescent-dyed latex particles coated with anti-TnI antibodies bind to TnI, if present in the sample. As the sample migrates along the strip, TnI bound particles are immobilized at the detection zone, and additional particles are immobilized at the internal control zone.

The RAMP Reader then measures the amount of fluorescence emitted by the complexes bound at the detection zone and at the internal control zone. Using a ratio between the two fluorescence values, a quantitative reading is calculated.

5. Indication for Use

The RAMP Troponin I Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure cardiac troponin I levels in EDTA whole blood. Measurement of cardiac troponin I aids in the rapid diagnosis of acute myocardial infarction (AMI). The RAMP Troponin I Assay is intended to be used only to prioritize patient management for those suspected of AMI.

6. Comparison of Technological Characteristics

The RAMP Troponin I Assay, Triage Cardiac Panel (Triage) Troponin I, and Dade Dimension RxL (Dimension) Cardiac Troponin-I (Troponin I) Flex Assays are for the quantitative measurement of TnI in human whole blood (RAMP and Triage) or plasma (Triage and Dimension). All three immunoassays utilize the binding of TnI to specific antibodies and utilize light in their respective detection systems. Both the RAMP and Triage assays measure light production from a fluorescence reaction using a fluorometer while the Dimension measures the amount of colored product produced which is directly proportional to the concentration of TnI present in the patient sample. Both the RAMP Troponin I and the Triage Troponin I assays are quantitative immunochromatographic tests, whereas the Dimension Troponin I test is a sandwich enzyme immunoassay.

7. Summary of Studies

PERFORMANCE CHARACTERISTICS

PRECISION: The intra-assay and the inter-assay precision of the RAMP Troponin I Assay were determined by one operator assaying duplicates of two standards (1.05 and 5.01 ng/mL TnI) twice each day over 10 days. The mean, standard deviation and %CV were calculated for the predicted TnI at each concentration. Within run precision was 8.7% and 8.3% respectively. Total precision was 10.0% and 8.3% respectively. Low end precision was also determined by the same method using Plasma Standards of 0.09, 0.15, 0.22, 0.29, 0.40 and 0.70 ng/mL TnI. The assay concentration in standards where 10.0% or less CV is achieved was 0.21 ng/mL TnI and where 20.0% or less CV is achieved was 0.14

ng/mL TnI for within run precision. The assay concentration in standards where 10.0% or less CV is achieved was 0.26 ng/mL TnI and where 20.0% or less CV is achieved was 0.15 ng/mL TnI for total precision. Low end precision of the RAMP Troponin I Assay was also determined in EDTA whole blood with one operator assaying 10 replicates of each of 5 spiked TnI concentrations. The assay concentration in blood where 10.0% or less CV is achieved was 0.21 ng/mL TnI and where 20.0% or less CV is achieved was 0.10 ng/mL TnI.

LINEARITY and PERCENT RECOVERY: TnI antigen concentrations of 0.86, 1.72, 3.44, 6.88, 13.75, and 27.5 ng/mL were prepared in normal donor EDTA blood. The linearity and percent recovery were determined by assaying five replicates of each concentration and baseline. The mean, standard deviation and %CV were calculated for the predicted TnI at each concentration. Linear regression analysis of actual TnI concentration versus expected TnI concentration resulted with an R = 0.997 and a slope of 1.019 with an offset of 0.279. The recovery of spiked TnI antigen at the five concentrations was 0.82, 1.72, 3.65, 7.65, 15.78, and 27.51 ng/mL. Percent recovery of TnI ranged from 95 to 115% with an average of 105%.

HOOK EFFECT: There is no high dose hook effect in the RAMP Troponin I Assay up to the highest level tested (500 ng/mL TnI).

ANALYTICAL SENSITIVITY: The lower limit of detection (LLD) is defined as the analyte concentration corresponding to the mean (n=20) plus 2 standard deviations of the zero. The LLD is 0.03 ng/mL TnI. TnI levels in excess of 32 ng/mL are reported as greater than (>) 32 ng/mL.

ANALYTICAL SPECIFICITY: Potentially cross-reactive substances were evaluated by spiking different concentrations into blood. Skeletal Troponin I, Cardiac Troponin T and Cardiac Troponin C appear to have no significant cross-reactivity with the RAMP Troponin I Assay. HAMA, HAGA, HARA and RhF appear to have minimal cross-reactivity with the RAMP Troponin I Assay.

INTERFERENCE: Potentially interfering substances were evaluated by spiking different concentrations of potential interferents into EDTA blood with TnI added. Different blood samples were used for each potential interferent. Interference was evaluated by calculating the TnI concentration of potential interferent-spiked blood, expressed as a percentage of the TnI concentration of the unspiked (no potential interferent) blood sample. No evidence of cross-reactivity or interference was observed for hemoglobin, triglyceride, bilirubin, cholesterol, or heparin at levels of very high physiological concentrations, up to 1500 mg/dL, 3000mg/dL, 80 mg/dL, 500 mg/dL, and 66 IU/mL, respectively. No trend was observed in the TnI predictions as the concentration of potential interferent was increased.

CLINICAL PERFORMANCE

EXPECTED VALUES

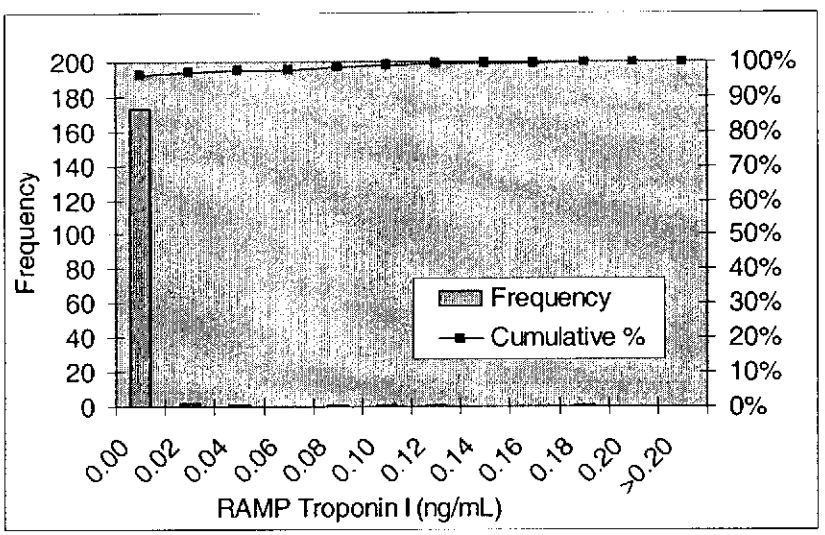
Whole blood samples from 180 healthy individuals (84 males and 96 females) were assayed for Troponin I by the three methods, RAMP, Triage, and Dimension. The lower (LLN) and upper (ULN) limits for normal range were defined as the 5^{th} and 95^{th} percentile values and are presented in Table 4-1. The RAMP Troponin I normal range distribution is presented in Figure 4-1.

The normal range of the RAMP Troponin I Assay was found to be 0.00 ng/mL in the normal population studied. The Triage system reports values less than 0.2 as "< 0.2" and because of this the normal range of the Triage Troponin I Assay was found to be < 0.2 ng/mL in the normal population studied. This is very similar to the normal range described in the Triage Troponin I package insert of < 0.19 ng/mL [1]. Finally, the Dimension normal range was found to be 0.00 to 0.04 ng/mL in the normal population studied. This is very similar to the normal range described in the Dimension Troponin I package insert of 0.00 to 0.05 ng/mL [2]. The data is presented in Table 4-1.

Table 4-1: Percentile Ranking of Normal Individuals

	RAMP	Triage	Dimension
Percentile	**ng/mL**	**ng/mL**	**ng/mL**
5th (LLN)	0.00	< 0.2	0.00
50th	0.00	< 0.2	0.00
90th	0.00	< 0.2	0.04
95th (ULN)	0.00	< 0.2	0.04
97.5th	0.025	< 0.2	0.04
Figure	11-1	11-2	11-3

Figure 4-1: RAMP Normal Range Distribution



PRECISION STUDY

One hundred and eighty-four (184) subjects were enrolled in the Precision Study. Of these, 55 were normal individuals (28 males and 27 females) and 129 were patients suspected of AMI based on the individual hospital criteria (76 males and 53 females). The samples were selected from those obtained during the Method Comparison Study. The samples were stored refrigerated for up to one day between analyses. The data were reviewed and one outlier was removed. Correlation for Troponin I Assay replicate Result 2 vs Result 1 for the RAMP Assay is presented in Table 4-2.

Table 4-2: Precision of RAMP Troponin I Assay, Result 1 vs Result 2

Population	n	Slope y =	Intercept	R
Combined Populations	183	1.086	-0.153	0.989
Patients with suspect AMI	128	1.093	-0.246	0.988

METHOD COMPARISON

Three hundred and sixty-five (365) subjects were enrolled in the Method Comparison Study. Of these subjects, 180 were normal individuals (84 males and 96 females) and 185 were suspected of acute myocardial infarct (AMI) based on the individual hospital criteria (115 males and 70 females). EDTA and heparin whole blood samples were obtained for each of these subjects. All normal subjects were consented. Waste samples were used for the subjects suspected of AMI. An aliquot of the whole blood was taken for the RAMP Troponin I Assay and heparinized plasma was prepared for the Triage Troponin I Assay and the Dimension Troponin I Assay. The samples were stored refrigerated for up to one day between analyses for the rapid tests. Heparin samples were frozen and sent to a reference lab for the Dimension testing.

To accommodate the differing reportable ranges of the RAMP and Triage Troponin I Assays, and the Dimension Troponin I Assay, the data were winsorized, and then examined for outliers. The correlation data is presented for both the RAMP and Triage Troponin I Assays versus the Dimension Troponin I Assay in Table 4-3.

Table 4-3: Correlation of RAMP and Triage vs Dimension

	Population	n	Slope (y =)	Intercept	R
RAMP Troponin I Assay					
	Combined Normal and Suspect AMI Subjects	364	0.456	0.011	0.988
	Suspect AMI Subjects	184	0.456	0.025	0.986
Triage Troponin I Assay					
	Combined Normal and Suspect AMI Subjects	365	0.718	- 0.138	0.974
	Suspect AMI Subjects	185	0.729	- 0.563	0.972

8. Conclusion

The RAMP Troponin I Assay when utilized with the RAMP Reader is substantially equivalent to other assays currently in commercial distribution for the measurement of TnI.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
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MAY 17 2004

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Re: k033745
Trade/Device Name: RAMP Troponin 1 Assay
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine phosphokinase/creatine kinase or isoenzymes test system
Regulatory Class: Class II
Product Code: MMI
Dated: March 15, 2004
Received: March 15, 2004

Dear Mr. Radvak:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Jean M. Cooper MS, DVM.

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Director
Division of Chemistry and Toxicology
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Enclosure

Indications for Use

510(k) Number (if known): K033745

Device Name: RAMP Troponin I Assay

Indications For Use: The RAMP Troponin I Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure cardiac troponin I levels in EDTA whole blood. Measurement of cardiac troponin I aids in the rapid diagnosis of acute myocardial infarction (AMI). The RAMP Troponin I Assay is intended to be used only to prioritize patient management for those suspected of AMI.

Prescription Use X (IVD) AND/OR Over-The-Counter Use N/A
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K033745